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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/723,626 | 11/26/2003 | Daniel Pratt | 19043-501 | 9707 |

30623 7590 06/02/2006

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| EXAMINER | |
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| ALSTRUM ACEVEDO, JAMES HENRY | |
| **ART UNIT** | **PAPER NUMBER** |
| 1616 | |

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/723,626 | PRATT ET AL. | |
| | Examiner | Art Unit | |
| | James H. Alstrum-Acevedo | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 4-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 and 4-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

**Claims 1-2 and 4-41 are pending.**

### *Drawings*

The objection to the drawings because the text in Figure 2 is difficult to read **is withdrawn**, because a readable version of said Figure has been submitted.

### *Specification*

The objection due to the incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication **is withdrawn**; because Applicant has amended the disclosure to include the material incorporated by reference.

The objection to the disclosure due to informalities described in the first office action on page 4 **is withdrawn**, because Applicant has amended the disclosure to correct said informalities.

The objection of claims 19, 21, 25, and 28 due to informalities described in the first office action on page 4 **is withdrawn**, because Applicant has amended the claims to correct said informalities.

The objection to the specification for the use of uncapitalized trademarks described on page 4 of the previous office action **is withdrawn**, because Applicant has amended the disclosure to include trademarks spelled with all capital letters

*Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

The rejection of claims 13-15, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is maintained**, because there is insufficient antecedent basis for the recited limitation "the ratio" in line 1 of said claims. It is noted that the words "said" and "the" are interchangeable. Therefore, amending the claims to read "the ratio" instead of "said ratio" does not correct the lack of antecedent basis.

The rejection of claims 16, 19-21, 25, 26, 28, and 29 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention as described in the previous office action on pages 4-6 **is withdrawn**, due to Applicant's amendments to said claims.

*Claim Rejections - 35 USC § 102*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejections of claims 1-2, 5, and 9 under 35 U.S.C. 102(b) as being anticipated by Patton et al. (U.S. Patent No. 5,814,607); claims 1-2, 5, 9, 16, and 20 under 35 U.S.C. 102(b) as being anticipated by Pitt et al. (U.S. Patent No. 5,354,934); and claims 1-2, 5, 9, 16, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Nissen et al. (U.S. Patent No.

US2002/0142964 A1) **are withdrawn**, due to Applicant's amendments to the claims. It is noted that claim 3 was cancelled by the Applicant.

The rejection of claims 1-2, 6, 16, 17, 19, 20, 33 under 35 U.S.C. 102(e) as being anticipated by Ouadji (U.S. Patent Application US2003/0138486) **is withdrawn**, per Applicant's amendments and persuasive arguments.

**Claims 1-2, 6, 10, 16, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Penners et al. (US Patent No. 6,306,439) (USPN '439).**

Applicant claims a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or oil and is controllably buoyant in the cerebrospinal fluid (CSF).

In claim 1 of USPN '439, Penners discloses a pharmacologically active composition in a physical form imparting a prolonged gastric residence time, said physical form being selected from the group consisting of **tablets, capsules, granules and pellets**, said composition comprising: (I) **at least one pharmacologically active compound**, (II) at least one pharmacologically acceptable auxiliary, (III) **polyvinylpyrrolidone (polymer)**, (IV) **a carboxymethyl cellulose polymer (i.e. a biodegradable polymer)** having an acidic number between 100 and 1,200 mg of KOH/g of polymer solid substance, and (V) optionally a **gas-forming additive**, the polymers (III) and (IV) being present in the form of a homogeneous mixture on the molecular level, the mixture being present in 30-90% by weight of the composition, the weight ratio of (III):(IV) ranging from 80:20 to 95:5, and the composition in dry compressed state being able to absorb many times its weight of acidic water thereby to form a highly swollen gel of high mechanical and dimensional stability capable of improved

prolonged release of the pharmacologically active compound. Pellets, granules, capsules, and tablets read on the term particle, per Applicant's definition of said term on page 6 of the specification to mean "a three-dimensional structure."

Penners discloses that suitable gas-forming agents (V) which can optionally be employed to increase the buoyancy are all substances which, **in contact with water** or gastric fluid, are able to form non-toxic gases. Examples are **hydrogen carbonates such as, for example, sodium hydrogen carbonate** (i.e. sodium bicarbonate), which are employed individually, or in combination with acids. **The gas, which forms, is incorporated into the hydrated gel layer as bubbles and thus contributes to the buoyancy of the tablet**.

Penners discloses an exemplary composition in Example 5, which comprises ciprofloxacin-HCl (antibiotic drug), gel mixture prepared according to Example 1 (contains polymer), and sodium bicarbonate (i.e. a sodium hydrogen carbonate). Penners composition inherently comprises a gas contained within a polymer particle, because, upon contact with water or another aqueous fluid (e.g. the cerebrospinal fluid (CSF)), sodium bicarbonate will decompose to generate carbon dioxide, which would contribute to the particle's buoyancy. Regarding the specific gravity of carbon dioxide, carbon dioxide is a gas at physiologic temperatures and has a density of $1.977 \times 10^{-3}$ g/mL at zero degrees, and therefore a specific gravity of $1.977 \times 10^{-3}$ or less (*CRC Handbook of Chemistry and Physics, 75th edition*, CRC Press: Boca Raton, 1994-1995, pp 4-50) (the calculation of specific gravity was described in the previous office action on page 8). Carboxymethyl cellulose polymer is a species of cellulose polymer and species anticipate the genus (i.e. cellulose).

*Claim Rejections - 35 USC § 103*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejections of claims 1-2, 4-10, and 12-31 under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Ouadji (U.S. Patent Application US2003/0138486); claim 11 under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Ouadji (U.S. Patent Application US2003/0138486) as applied to claims 1-2, 4-10, and 12-31 above, and further in view of Chen et al. (*Proceedings of the National Academy of Science*, 2002, *99(13)*, 9031-9036); and claim 32 under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Ouadji (U.S. Patent Application US2003/0138486), in further view of Chen et al. (*Proceedings of the National Academy of Science*, 2002, *99(13)*, 9031-9036) as applied to claims 1, 2, and 4-31 above, and further in view of Hatcher et al. (Society for Neuroscience, 19th Annual Meeting, Abstract #236.4, Oct. 23-28, 1999) **are withdrawn**, due to Applicant's amendments and persuasive arguments.

**Claims 12-31, 35, 37-38, and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Penners et al. (US Patent No. 6,306,439) (USPN '439).**

*Applicant Claims*

Applicant recites (1) a first and second polymer particle, wherein each particle comprises a first and second therapeutic agent, respectively, and a buoyancy agent, wherein the buoyancy agent is selected from gases and oils and is controllably buoyant within the CSF and (2) a

method of administering a therapeutic agent within the central nervous system (CNS) comprising intrathecal administration of a composition to a subject's CNS, wherein said composition comprises a biodegradable polymer having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is selected from gases and oils and is controllably buoyant within the CSF.

***Determination of the Scope and Content of the Prior Art*** (MPEP §2141.01)

The teachings of Penners have been set forth above in the rejection of claims 1-2, 6, 10, 16, and 34 under 35 U.S.C. 102(b). The teachings of Kim were set forth in the previous office action, but are recited herein for ease of reference. Kim teaches a method for **treating a neurological disorder** using a slow-release vehicle .for delivery of a **therapeutic agent** to the **cerebrospinal fluid (CSF)** of a human (column 1, lines 8-11) and that the surprising ability of the therapeutic agent **to ameliorate the neurological disorder** is due to the presentation of the therapeutic agent in a dispersion system, which **allows the agent to persist** in the cerebro-ventricular space (column 2, lines 34-36). Kim defines a **neurological disorder** as any disorder that is present in the brain, spinal column, and related tissues, which are responsive to an appropriate therapeutic agent, including meninges and cell proliferative diseases (column 2, lines 42-48). Specific examples of these disorders include tumors that metastically infiltrate the leptomeninges, including non-Hodgkin's lymphoma, leukemia, melanoma (col. 2, lines 65-67) as well as those disorders resulting from infections such as aseptic meningitis, encephalitis, Lentivirus, HIV, various bacterial infections, etc (col. 3, lines 1-22).

Suitable therapeutic agents are administered to the CSF in a delivery system such as **synthetic or natural polymers** in the form of macromolecular complexes, nanocapsules, microspheres, etc., collectively known as dispersion systems. The particles comprising the system are about **20 nm to 50 μm in diameter**. These dispersions may be administered intraventricularly, **intrathecally**, preferably by an injection of the particles by intralumbar puncture (column 3, lines 23-35). In one class of dispersion the therapeutic agent is released from a polymer matrix made from synthetic polymers including, **polyesters**, **polyurethanes**, **polyorthoesters**, and **polyanhydrides**. Regarding polyesters, **PLA and PLA/PGA polyesters** are cited as examples that have been extensively studied for use as polymer matrices of therapeutic agents. PLA, PGA, and PLA/PGA are poly(lactide), poly(glycolide), and poly(lactide-co-glycolide), respectively (column 3, lines 64-67 and column 4, lines 1-3). Kim states that the term "**therapeutic agent**" as used includes, without limitation, **drugs, radioisotopes**, and **immunomodulators**. The term "drugs" includes "non-proteinaceous" and "proteinaceous" drugs. "Non-proteinaceous" drugs include, for example, mitomycin C, daunorubicin, AZT, **hormones**, and 5-flurouracil. Estrogen is an art-recognized hormone. "Proteinaceous" drugs include **immunomodulators** and other biological responsive modifiers as well as **antibodies**, with an example being lymphokines (column 6, lines 9-11 and 23-53). Antibodies can also be used in **combination with other therapeutic agents** (column 7, lines 40-41). Examples of **radioisotopes to treat cell proliferative disorders (i.e. radiopharmaceuticals)** include $^{125}I$, $^{131}I$, $^{90}Y$, $^{67}Cu$, $^{212}Bi$, $^{211}At$, $^{212}Pb$, $^{47}Sc$, $^{109}Pd$, and $^{188}Re$ (column 6, lines 54-67 and column 7, lines 1-3). Kim teaches that materials used in the dispersion are sterilizable including, albumin, **ethylcellulose, casein, gelatin**, and **soybean oil**

(column 3, lines 37-40). The dispersion system density may be modified by **altering the specific gravity** to make the dispersion hyperbaric or hypobaric by addition of biocompatible molecules with high specific gravity (column 3, lines 43-49).

Kim teaches the solid polymeric dispersion system can be produced initially as a larger mass, which is then ground, or otherwise processed, into particles small enough to maintain a dispersion in the appropriate physiologic buffer (column 4, lines 14-19).

Kim teaches that the **exact dosages of therapeutic agents used will vary** depending upon such factors as the particular therapeutic agent and desirable medical effect, as well as patient factors such as age, sex, general condition and the like. Those of skill in the art can readily take these factors into account and use them to establish effective therapeutic concentrations without resort to undue experimentation (column 8, lines 13-19).

***Ascertainment of the Difference Between Scope the Prior Art and the Claims***

***(MPEP §2141.012)***

Kim lacks the teaching of a specific buoyancy agent. This deficiency is cured by Penners' teachings.

***Finding of Prima Facie Obviousness Rational and Motivation***

***(MPEP §2142-2143)***

It would have been obvious to a person of ordinary skill at the time of the instant invention to combine the teachings of Kim and Penners, because both inventors teach dispersible pharmaceutical compositions comprising therapeutic agents and polymers, which have

controlled-release or sustained-release properties. A skilled artisan would have been motivated to combine the teachings of Kim and Penners, to affect the density of Kim's formulations through the use of buoyancy agents, including formulations that would generate $CO_2$ gas *in situ* upon degradation of the polymer matrix (e.g. compositions comprising sodium bicarbonate and citric acid), and because Penners teaches that the gas-forming substances in his composition evolve non-toxic gases upon contact with water. Cerebral spinal fluid (CSF) is an aqueous medium. A skilled artisan would have had a reasonable expectation of success, upon combination of the prior art teachings, that contact of Penners' compositions with CSF, as used in the method of Kim, would yield controllably buoyant particles upon decomposition of the gas generating substance (e.g. sodium bicarbonate decomposing to form carbon dioxide). Furthermore, it would have been obvious to a skilled artisan that one could lower a formulation's specific gravity by the inclusion of any pharmaceutically acceptable gas (e.g. $O_2$, $N_2$, Ar, He, Ne, or Xe) or mixture thereof (e.g. air is a mixture of $N_2$ and $O_2$) in said formulation, because it is well known that gases have much lower densities than either solids or liquids (see Brown, T. L. *Chemistry: The Central Science, 6th ed.* Prentice Hall: Englewood Cliffs, NJ, 1994, p 18 (provided with the last office action). It also would have been obvious to a person of ordinary skill in the art to vary the specific gravity of biocompatible compositions through routine optimization practiced in the art. Regarding claim 12, it would have been obvious to a person of ordinary skill to use two different polymer particles, each containing a different therapeutic agent, because Kim teaches that antibodies (a proteinaceous drug) can be used in combination with other therapeutic agents. Modulating the ratio of the quantities of the first and second polymeric particles is essentially modifying the dosages of the therapeutic agents contained

within each particle. Claims 13-15 would have been obvious to a skilled artisan at the time of the instant invention, because the variation of different therapeutic agent dosages in a composition would have been achieved through the routine optimization of pharmaceutical formulations to adjust the therapy to the particular needs and symptoms of a patient.

**Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Penners et al. (US Patent No. 6,306,439) (USPN '439) as applied to claims 1-2, 4-10, 12-31, and 35 above, and further in view of Chen et al. ("Inosine Induces Axonal Rewiring and Improves Behavioral Outcome After Stroke," *Proceedings of the National Academy of Science*, 2002, *99(13)*, 9031-9036).**

*Applicant Claims*

Applicant claims a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or oil and is controllably buoyant in the cerebrospinal fluid (CSF), and wherein the therapeutic agent is selected from the group consisting of inosine, citicholine, superoxide dismutase (SOD), and dextrophan.

***Determination of the Scope and Content of the Prior Art (MPEP §2141.01)***

The teachings of Kim and Penners have been set forth above in the instant office action. The teachings of Chen were set forth in the previous office action, but are repeated herein for ease of reference. Chen teaches that the administration of **inosine** to rats with **unilateral**

**cortical infarcts** (i.e. strokes) resulted in the stimulation of neurons on the undamaged side of the brain to extend new projections to denervated areas of the midbrain and spinal cord. This growth was paralleled by improved performance on several behavioral measures (abstract, last sentence).

Chen states that it is known in the art that inosine regulates the expression of multiple genes involved in axon growth, in at least some neurons, and in vivo inosine treatment can promote extensive sprouting of the intact corticospinal tract (CST) into areas denervated by transecting the contralateral CST (p 9031, left hand column, 2nd paragraph).

Chen states "these studies show that inosine induces significant axonal reorganization in the rat brain after stroke and helps restore cortical control of the denervated forelimb" (page 9035, left hand column, 1st sentence in the Discussion).

Chen states that in animal models antioxidants, caspase inhibitors, glutamate receptor blockers, and other agents improve functional outcome after stroke by inhibiting cell death (p 9035, right hand column, last paragraph before the acknowledgements).

Chen concludes that inosine does not appear to exert neuroprotective effects, however because its effect on stimulating axonal rewiring are **complementary** to those of neuroprotective agents and inosine treatment **may represent a novel approach to improving function after stroke or CNS trauma** (p 9035, right hand column, last paragraph before the acknowledgements).

***Ascertainment of the Difference Between Scope the Prior Art and the Claims***

***(MPEP §2141.012)***

Both Kim and Penners lack the teaching of a biocompatible composition wherein the therapeutic agent is selected from the group consisting of inosine, citicholine, superoxide dismutase (SOD), and dextrophan. This deficiency is cured by the teachings of Chen.

***Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)***

It would have been obvious to a person of ordinary skill in the art to combine the teachings of Kim & Penners with those of Chen in a therapeutic composition intended for the treatment of a neurological disorder resulting from stroke or CNS trauma because inosine stimulates axonal rewiring, which is complementary to the effect of neuroprotective agents, such as antioxidants and glutamate receptor blockers. Furthermore, the combined teachings of Kim & Penners teach dispersible pharmaceutical compositions with sustained release properties for the treatment of neurological disorders. A skilled artisan would have been motivated to use inosine, because its stimulatory effect on axonal growth has been demonstrated in rats, and thereby providing said artisan with a reasonable expectation of success for the treatment of neurological disorders resulting from stroke or CNS trauma.

**Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Penners et al. (US Patent No. 6,306,439) (USPN '439), in view of Chen et al. (*Proceedings of the National Academy of Science*, 2002, *99(13)*, 9031-9036) as applied to claims 1-2, 4-31, and 35 above, and further in view of Hatcher et al. (Society for Neuroscience, 19th Annual Meeting, Abstract #236.4, Oct. 23-28, 1999).**

*Applicant Claims*

Applicant claims a biocompatible composition as described above in the rejection of claims 12-31 and 35 are rejected under 35 U.S.C. 103(a) further comprising a first and second polymer particle having a first and second therapeutic agent, wherein the first therapeutic agent is inosine and the second therapeutic agent is citicholine.

***Determination of the Scope and Content of the Prior Art*** (MPEP §2141.01)

The teachings of Kim, Penners, and Chen have been set forth above in the instant office action. Hatcher teaches CDP-choline (also known as citicholine) significantly decreased neuronal death to 31 ± 6% when ischemic duration was increased to 10 minutes and that two doses of citicholine (at 0 and 1 day) provided slight **neuroprotection** (abstract only)

***Ascertainment of the Difference Between Scope the Prior Art and the Claims***

***(MPEP §2141.012)***

Kim, Penners, and Chen lack the teaching of a composition comprising both inosine and citicholine as therapeutic agents. This deficiency is cured by the teachings of Hatcher.

***Finding of Prima Facie Obviousness Rational and Motivation***
***(MPEP §2142-2143)***

It would have been obvious to a person of ordinary skill at the time of the instant invention to use inosine and citicholine in the same pharmaceutical compositions, because Chen teaches that inosine's effect on stimulating axonal rewiring are **complementary** to those of neuroprotective agents. A skilled artisan would have been motivated to combine the teachings of

Kim, Penners, Chen, and Hatcher, due to the complementary nature of inosine's pharmacological effects to those of neuroprotective agents. A person of ordinary skill in the art would have been further motivated to combine the teachings of the aforementioned prior art with the teachings of Hatcher, because citicholine has neuroprotective properties and Chen suggests inosine treatment may represent a novel approach to improving function after stroke or CNS trauma. A skilled artisan would have had a reasonable expectation of successfully combining inosine and citicholine to obtain a pharmaceutical composition appropriate for the treatment of neurological disorders for the above-mentioned reasons.

**Claims 36 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (U.S. Patent No. 5,455,044) in view of Penners et al. (US Patent No. 6,306,439) (USPN '439) as applied to claim 12-31, 35, 37-38, and 40-41 above, and further in view of Russell et al. ("Allogenic Blood Stem Cells and Bone Marrow Transplantation for Acute Myelogenous Leukemia and Myelodysplasia: Influence of Stem Cell Source on Outcome," Bone Marrow Transplantation, 1999, 24, 1177-1183).**

*Applicant Claims*

Applicant recited (a) a composition of claim 19, wherein the therapeutic agent comprises living cells selected from bone marrow cells and fetal neural tissue or stem cells and (b) the method of claim 25, wherein the therapeutic agent comprises living cells selected from bone marrow cells and fetal neural tissue or stem cells.

***Determination of the Scope and Content of the Prior Art (MPEP §2141.01)***

The teachings of Kim and Penners have been set forth above in the instant office action. Russell is provided herein to demonstrate that living cells, specifically bone marrow stem cells and blood cell stem cells, are art recognized therapeutic agents used in the treatment of leukemia. Russell teaches comparative studies of the treatment of patients with acute myelogenous leukemia (AML) and Myelodysplasia (MDS) who received sibling transplants with stem cells from peripheral blood (blood cell transplant, BCT) or bone marrow (BMT). Russell concluded by stating that while disease-free survival may be better using BCT than BMT for AML, it may greatly impair quality of life, due to a higher proportion of acute graft-versus-host disease (GVHD) (abstract).

***Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)***

Kim and Penners lack the teaching of living cells as therapeutic agents. This deficiency is cured by the teachings of Russell.

***Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)***

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Kim, Penners, and Russell, because Kim teaches compositions and methods, which can be used in the treatment of cell proliferative diseases, including leukemia and Russell discloses two treatments of leukemia comprising the administration of living cells as therapeutic agents. It would have been obvious to a person of

ordinary skill in the art at the time of the instant invention who was cognizant of the teachings of Russell that living cells, particularly bone marrow and red blood stem cells, are known therapeutic agents for the treatment of leukemia and myelodysplasia. A skilled artisan would have been motivated to include bone marrow and/or blood stem cells in the therapeutic compositions and methods taught by Kim, because leukemia is a specific disease taught as being treatable by Kim's compositions and methods (col. 2, lines 65-67). A skilled artisan would have had a reasonable expectation of success upon combination of Russell's teachings with those of Kim and Penners, because bone marrow stem cells and blood stem cells are known therapeutic agents used in the treatment of leukemia.

***Conclusion***

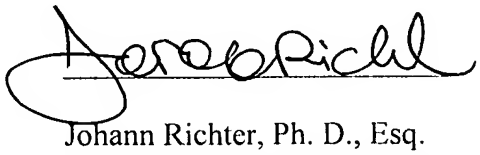
**Claims 1-2 and 4-41 are rejected. No claims are allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0664. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James H. Alstrum-Acevedo, Ph.D.
Patent Examiner
Technology Center 1600



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